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2004 WL 77420 (Bd.Pat.App. & Interf.)

Board of Patent Appeals and Interferences
Patent and Trademark Office (P.T.O.)

*1 EX PARTE JOACHIM
GANTE
, HORST JURASZYK, PETER RADDATZ, HANNS WURZIGER, SABINE BERNOTAT-DANIELOWSKI, GUIDO MELZER, MATTHIAS WIESNER AND CLAUS FITTSCHEN

Appeal 1999-1686
Application 08/552,206
[FN1]

NO DATE REFERENCE AVAILABLE FOR THIS DOCUMENT

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Before: STONER
Chief Administrative Patent Judge

WILLIAM F. SMITH
Administrative Patent Judge

McKELVEY
Senior Administrative Patent Judge
McKELVEY
Senior Administrative Patent Judge

Decision on appeal under 35 U.S.C. § 134

The appeal is from a decision of a primary examiner rejecting claims 1-3, 6-9, 15-16, 23 and 26. The examiner entered three rejections. We reverse two rejections and we vacate and remand as to the third rejection.

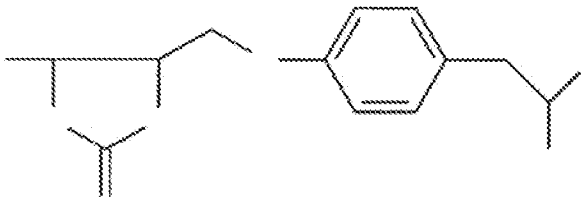
A. Findings of fact
The record supports the following findings by at least a preponderance of the evidence.[FN2]

The claimed invention

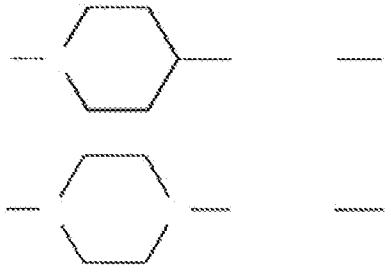
1. Claims 1-3, 6-9, 15-16, 23 and 26 are on appeal.

2. Claim 1 is the only independent claim and is the broadest claim on appeal. It reads:

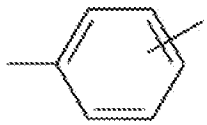
An oxazolidinone compound of formula I



wherein R^1 is



or



R^2 is H [hydrogen], A, Ac, A-SO2-, Ar-SO2-, or an amino protective group;
R^3 is H, A, cycloalkyl having 3 to 7 C [carbon] atoms, Ar or Ar)(CH2) k-;
A is alkyl having 1 to 16 C atoms;
B is H, A or H2N-C(=NH)-;
D is H2N-CH2-, H2N=C(=NH)- or H2N-C(=NH)-NH-CH2-, wherein primary amino groups in each case can optionally be provided with amino protective groups;
Ac is alkanoyl having 1 to 10 C atoms or aroyl having 7 to 11 C atoms;
Ar is benzyl, unsubstituted phenyl or phenyl which is mono- or disubstituted by A, Cl, Br, I, OA, OH, NO2, CN, NH2, NHA, NA2 or combinations thereof;
m is 0, 1, 2, 3 or 4;
n is 2, 3 or 4; and
k is 2, 3 or 4; or a physiologically acceptable salt thereof.

3. Claim 2 depends from claim 1 and reads:
A compound according to claim 1, wherein said compound is an enantiomer.

4. Claim 3 depends from claim 2 and reads:
A diastereomeric compound formed by reacting a compound according to claim 2 with an optically active re-

solving agent.

Applicants' specification

4. The compounds of formula I are said to have "useful properties, in particular those which can be used for the production of medicaments" (specification, page 2, lines 6-8).

5. According to applicants (specification, page 2, lines 12-15):
It was found that the compounds of formula I, and their solvates and salts, have useful pharmacological properties together with good tolerability.

*2 6. Further according to applicants (specification, page 2, lines 15-21):
The compounds have integrin inhibiting effects, in particular they inhibit interaction of <<beta>>3- or <<beta>>5- integrin receptors with ligands. Especially, they affect the av<<beta>>3, av<<beta>>5 and aIIb<<beta>>3 integrins. The activity of the compounds can be demonstrated, for example, by the method of J.W. Smith et al., described in J. Biol. Chem. 265:12267-12271 (1990).

7. Still further according to applicants (specification, page 2, lines 21 through page 3, line 14):
In particular, they [, i.e., the compounds of formula I,] inhibit the binding of fibrinogen, fibronectin and of the von Willebrand factor to the fibrinogen receptor of the blood platelets (glycoprotein IIb/IIIa) and also the binding thereof and of further adhesive proteins, such as vitronectin, collagen and laminin, to the corresponding receptors on the surface of various cell types. The compounds thus affect cell-cell and cell-matrix interactions. In particular, they prevent the formation of blood platelet thrombi and can therefore be used for treatment of thromboses, apoplexia, cardiac infarct, angina pectoris, osteolytic diseases, in particular osteoporosis, anti-angiogenesis and restenosis after angioplasty, ischaemias, inflammations, arteriosclerosis and of acute kidney failure. The compounds also have an effect on tumor cells by inhibiting their metastasization. They can thus also be employed as antitumor agents.
There are indications that tumor cells pass into the vessels by means of microthrombi and are thus protected from detection by cells of the immune system. Micro-thrombi also have a supportive effect on the binding of tumor cells to the vessel walls. Since the formation of the microthrombi is connected with the fibrinogen binding to the fibrinogen receptor (glycoprotein IIb/IIIa), fibrinogen binding inhibitors likewise count [, i.e., can be used,] as metastasis inhibitors.

8. Applicants go on to state (specification, page 3, lines 15-23):
Also, since fibrinogen-binding inhibitors are ligands with fibrinogen receptor on platelets, they can be used as diagnostic tools for detection and localization of thrombi in the vascular in vivo. Thus, for example, in accordance with known procedures, the fibrinogen-binding inhibitors can be labelled with a signal generating or detectable moiety whereby, once the labeled fibrinogen-binding inhibitor is bound to a fibrinogen receptor on platelets, it is possible to detect and locate thrombi.

9. Applicants continue (specification, page 3, line 24 through page 3a, line 21):
Fibrinogen-binding inhibitors are also very effective as research tools for studying the metabolism of platelets in the different activation states or intracellular signalling mechanisms of the fibrinogen receptor. For example, as described above, fibrinogen-binding inhibitor can be labeled with a signal generating or detectable moiety. The fibrinogen-binding inhibitor-signal generating/detectable moiety conjugate can then be employed in vitro as a research tool. By binding the conjugate to fibrinogen receptors, it is possible to monitor and study the metabolism of platelets, as well as the activation states and signalling mechanisms of the fibrinogen receptors.
*3 The compounds [of formula I] are additionally suitable as antimicrobial agents which can prevent infections, such as can be caused, for example, by bacteria, fungi or yeasts. The substances can therefore preferably be given as accompanying antimicrobial agents when operations on bodies are performed in which exogenous substances,

such as biomaterials, implants, catheters or cardiac pacemakers, are employed. They act as antiseptics. Antimicrobial activities of the compound can be demonstrated, for example, by the method of P. Valentin-Weigand et al., described in Infection and Immunity, 2851-2855 (1988).
The other properties of the compounds can be demonstrated by methods which are described in EP-A1-0 462 960. The inhibition of fibrin binding to the fibrinogen receptor can be demonstrated by the method which is indicated in EP-A1-0 381 033. The platelet aggregation-inhibiting action can be demonstrated in vitro by the method of Born (Nature, 4832:927-929 (1962)).

10. With respect to claim 3 calling for forming a diastereomeric compound using "an optically active resolving agent", the specification (page 15, line 39 through page 16, line 12) reveals:

*** [D]iastereomers are formed from *** [a] racemic mixture by reaction with an optically active resolving agent. Suitable resolving agents are, for example, optically active acids, such as the D- and L-forms of tartaric acid, diacetyltartaric acid, dibenzoyltartaric acid, mandelic acid, malic acid, lactic acid or the various optically active camphorsulfonic acids such as <<beta>>-camphorsulfonic acid. Resolution of the enantiomers with the aid of a column packed with an optically active resolving agent (e.g. dinitrobenzoyl-phenylglycine) is also advantageous; a suitable eluent is, for example, a hexane/isopropanol/acetonitrile mixture, e.g. in the volume ratio 82:15:3.

The examiner's rejections

11. The examiner entered three rejections.

12. Claims 1-4, 6-10, 15-16, 23 and 26 were rejected under 35 U.S.C. § 103(a) as being unpatentable over (1) **Gante**, U.S. Patent 5,561,148 (1996, filed 22 September 1994) and (2) Yano, U.S. Patent 5,480,899 (1996, filed 28 April 1993).

13. Claims 1-3, 10, and 15-16 were rejected "under judicial doctrine as drawn to an improper Markush group ***."

14. Claims 1-3, 6-9, 15-16, 23 and 26 were rejected under the first paragraph of 35 U.S.C. § 112 on the ground of an alleged lack of an enabling description of how to make enantiomers and under the second paragraph of 35 U.S.C. § 112 on the ground that the term "aroyl" (see, e.g., Claim 1) is indefinite.

B. Discussion

1. Rejection based on the prior art

*4 We agree with the following observation in applicants' Reply Brief (page 1): "the Examiner's Answer is most difficult to read and understand ***." Applicants go on to say that remarks in their Reply Brief constitute their best "attempt to decipher the incomplete sentences and cryptic citations to one or another of the cited references, which [citations] are often without attribution to a particular location [, i.e., col. and line,] in the reference ***."

The examiner maintains that **Gante** and Yano somehow make out a prima facie case of obviousness. The examiner, however, has not explained how the prior art makes out a prima facie case. For example, the examiner did not follow the guidelines set out in § 706.02(j) of the Manual of Patent Examining Procedure.

Based on our independent review of the prior art, we find that a case of obviousness can be made out only by referring to, and being guided by, information contained in applicants' specification. What that means is that the examiner's case of obviousness is bottomed on impermissible hindsight. In re McLaughlin, 443 F.2d 1392, 1395, 170 USPQ 209, 212 (CCPA 1971). Accordingly, the decision of the examiner rejecting claims 1-4, 6-10, 15-16, 23 and 26 under 35 U.S.C. § 103(a) as being unpatentable over **Gante** and Yano is reversed.

2. Rejections based on 35 U.S.C. § 112

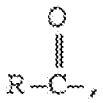
The examiner's rationale with respect to the § 112 rejections is as difficult to decipher as is the rationale in support of the rejection based on § 103.

a.

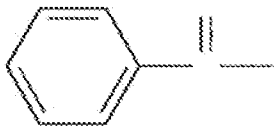
The examiner apparently believes that the term "aroyl" is indefinite. For example, the examiner "asks" applicants to tell the Patent and Trademark Office (PTO) "[w]hat is 'aroyl' of 8, 9 or 10 carbons?" According to the examiner, applicants did not answer the question. The examiner may have a point, because it is not clear that applicants have favored the examiner or us with meaningful discussion on the point of the meaning of "aroyl".

Nevertheless, we find that "aroyl" is not an indefinite term in the context of the invention described in the specification. The phrase in dispute is the limitation in claim 1 that "Ac is alkanoyl having 1 to 10 C [carbon] atoms or aroyl having 7 to 11 C atoms.

A person of ordinary skill in the art knows that an alkanoyl group is one having an alkyl connected to a ketone group, e.g.,



where R is alkyl. An aroyl group is similar, except that the R is a phenyl group, e.g., benzoyl, which has the following structure:



The benzoyl aroyl shown has 7 carbon atoms, 6 of which are located in the ring structure. To answer the examiner's question, an aroyl having 8 carbon atoms might have the following structure:

***5** It is not difficult to imagine aroyls with 9 or 10, or for that matter 11, carbon atoms.

The examiner's indefiniteness rejection is reversed.

b.

The examiner had difficulty with the term "resolving agent." We do not understand why. In the specification, applicants set out (Finding 10) numerous resolving agents which can be used.

The examiner says that "resolving agent" is "improperly functional." Apart from the fact we are not sure what is meant

by "improperly functional," there is nothing inherently improper in defining an agent by the function it performs, in this case resolution of a racemic mixture into enantiomers.

Lastly, the examiner maintains that there is a lack of an enabling description of "how to use" the resolving agent. But, applicant tells us how to use a resolving agent to separate enantiomers (Finding 10).

The examiner's § 112 rejection related to "resolving agent" is reversed.

3. The "Markush" issue

The examiner's explanation of the basis for the "improper Markush group" rejection gives us pause. Rather than reverse the rejection, we believe it more appropriate to vacate the rejection and remand the application to the examiner for fact-finding in the first instance with respect to the Markush issue.

a.

The CCPA, in its last pronouncement on the issue,[FN3] indicates that the PTO has authority to make a rejection based on an improper Markush group. In re Harnisch, 631 F.2d 716, 720, 206 USPQ 300, 304 (col. 1) (CCPA 1980). But, as the CCPA noted, "there is not one [Markush] 'doctrine' or rule; there are many." Id. at 720, 206 USPQ at 304 (col. 1). Accordingly, the examiner's reference to "judicial doctrine" relating to improper Markush group rejections is not entirely accurate.

b.

What are some of these many rules to which the CCPA makes reference and what factors might appropriately be considered? We call attention to the following factors for consideration, in no particular order of importance.

Factor 1: In Harnisch the CCPA observed that the PTO has authority to determine whether the claims before the PTO are in proper form to be examined for patentability on the merits. Id. at 720 and 721, 206 USPQ 304 (col. 1) and 305 (col. 1). Is an application which claims more than one invention[FN4] in a single claim in proper form to be examined on the merits? If not, is it appropriate to reject the claim as containing an improper Markush group.

Factor 2: When considering the propriety of claims defining compounds or other inventions by Markush or other groups, the invention must be considered as a whole--e.g., not just a "Markush" part of compounds or the other invention. Harnisch, at 722, 206 USPQ at 305.

*6 Factor 3: In Harnisch, the CCPA indicates that unity of invention as a factor which might be considered. We are not entirely sure whether the CCPA refers to unity of invention within the meaning of Patent Cooperation Treaty practice or something else. Nevertheless, the CCPA discussed the following:

Factor 3a: In the case of compounds, do the compounds considered as a whole have a "community of properties"? Harnisch, at 722, 206 USPQ at 305. We would observe, that different compounds having a "community of properties," i.e., the same utility, may or may not be directed to a proper Markush group.

Factor 3b: In the case of compounds, do the compounds considered as a whole have a significant shared structural element? Again, we would observe that different compounds having significant shared structural elements may or may not be directed to a proper Markush group.

Factor 3c: Is the grouping of compounds "repugnant to principles of scientific classification"? Harnisch, at 722, 206

USPQ at 305. For example, an inventor of four inventions might present in a single application a description of each of the four inventions and a claim which reads:

An invention selected from the group consisting of
(1) a carburetor comprising elements 1, 2 and 3
or
(2) wrist watch comprising elements 4, 5 or 6
or
(3) a DNA having the structure shown in SEQ ID No. 4
or
(4) a method of polymerizing polyolefins comprising process steps 7, 8 and 9.
It is difficult to fit the four inventions into a classification which makes any "patent" or "scientific" sense.

Factor 4: Is the fact that an applicant claims priority under 35 U.S.C. § 119 of more than one foreign application relevant? We have not undertaken an analysis of the two German language applications in the file of the application on appeal to determine why two applications were filed in Germany and only one is being filed in the United States.

Factor 5: Each case is decided on its own facts and necessarily involves the exercise of reasoned discretion.

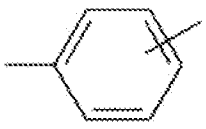
We readily acknowledge that there may be other relevant factors and that all factors might not apply in a particular case. Furthermore, we do not believe the CCPA in Harnisch attempted to list all factors.[FN5] Moreover, factors may come into existence as a result of (1) future experience, including future judicial and administrative decisions in particular cases, (2) amendments to the Patent Law or (3) amendments to PTO regulations. As we noted earlier, whatever the factors relevant to a particular case, a decision to reject a claim, as authorized by Harnisch, requires the exercise of informed discretion on a case-by-case basis.

c.

*7 While we have not undertaken a complete examination (see, e.g., 37 CFR § 1.104) of the subject matter of claim 1 on appeal, with respect to Factor 3a, we make the following observations on the basis of some of the prior art cited by the examiner during prosecution of this application.

(1)

Absent additional evidence in the record, it would appear that claim 1 on appeal covers at least two separately patentable inventions within the meaning of 37 CFR § 1.601(n) when only differences in the R^1 group are taken into account. For example, if one were to presume that prior art describes applicants' compounds wherein R^1 is the "phenyl" radical:



on what basis on this record could one reject applicants' compounds wherein R^1 is the "piperidinyl" radical:

assuming all other moieties are identical.

Gante, U.S. Patent 5,561,148, relied on by the examiner in connection with the rejection under § 103(a), describes an R^1 which is phenyl, but not piperidinyl. We will note, in this respect, that the examiner appears to have required applicant to elect species between inter alia the phenyl compounds and the piperidinyl compounds.[FN6] It is not apparent to us that other art in the record equates in a patentable sense phenyl groups in R^1 position with piperidinyl groups in that same position.

(2)

On this record, it also becomes manifest that compounds which may have a "community of properties" can be directed to separate patentable inventions. Take the **Gante** patent relied upon by the examiner in connection with the § 103(a) rejection. The compounds claimed in **Gante** are said to have what appears to be the same properties as those claimed in this application. In this respect, we call attention to the discussion from col. 1, line 45 to col. 2, line 49 which is virtually identical to the discussion in the specification on appeal (see Findings 4-9).

In the prior paragraph, it will be noted that we used the language "which may have". Our review of applicants' specification, gives us pause as to whether applicants are saying (1) that all the compounds of claim 1 have all the properties set out in the specification or (2) that all the compounds of claim 1 have at least one property set out in the specification. We would find it an astonishing accomplishment if all the compounds of claim 1 possessed all the properties set out in the specification. Certainly, there is no scientific experimental data reported in the specification upon which a reasoned finding could be made that all compounds possess all properties. We believe it more likely that applicants mean that all the compounds of claim 1 have at least one of the useful properties set out in the specification. Why do we say so?

*8 As noted in Finding 4, applicants tell us that:

> The compounds have integrin inhibiting effects, in particular they inhibit interaction of <<beta>>3- or <<beta>>5- integrin receptors with ligands. Especially, they affect the av<<beta>>3, av<<beta>>5 and aIIb<<beta>>3 integrins. The activity of the compounds can be demonstrated, for example, by the method of J.W. Smith et al., described in J. Biol. Chem. 265:12267-12271 (1990).

Applicants provide a method by which compounds can be tested to see if they have the inhibitory effect set out in the specification. The same is true with respect to other properties. Thus, a Valentin-Weigand procedure can be used for testing bacteria, fungi or yeast prevention. What is apparently a different Valentin-Weigand procedure may be used for testing for antimicrobial activity. A method set out in European Patent Application 0 381 033 can be used to test for inhibition of fibrin binding. Lastly, a Born procedure set out can be used to test for platelet aggregation-inhibiting action. See Finding 9. It may be that the compounds of claim 1 do not have a community of properties. On this record we are in no position to make findings on the properties of individual compounds within the scope of claim 1. The factual issue of whether all the compounds of claim 1 have the same utility is a matter to be looked into on remand.

4. Decision and order

Upon consideration of the appeal, and for the reasons given, it is

ORDERED that the examiner's rejection based on 35 U.S.C. § 103 is reversed.

FURTHER ORDERED that the examiner's rejections based on 35 U.S.C. § 112 are reversed.

FURTHER ORDERED that the examiner's rejection based on an improper Markush group is vacated.

FURTHER ORDERED that the application is remanded for such further action as may be appropriate.

FURTHER ORDERED that nothing in this opinion should be construed as precluding a further rejection of the claims based on (1) an improper Markush or other group or (2) prior art uncovered as a result of an examination on the merits of the R^1 embodiments of claim 1 which are not phenyl embodiments, matters on which we express no opinion on the merits.

FURTHER ORDERED that no time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

Reversed-in-part and vacated and remanded-in-part

BOARD OF PATENT APPEALS AND INTERFERECES

BRUCE H. STONER, Jr., Chief

Administrative Patent Judge

WILLIAM F. SMITH

Administrative Patent Judge

FRED E. McKELVEY, Senior

Administrative Patent Judge

FN1. Application for patent filed 2 November 1995. The real party in interest is Merck Patent GmBH. Applicants claim the benefit under 35 U.S.C. § 119 of German application P 44 39 110.2, filed 2 November 1994, and German application DE 1 95-09093.4, filed 16 March 1995.

FN2. To the extent these findings of fact discuss legal issues, they may be treated as conclusions of law.

FN3. Insofar as we are aware, the Federal Circuit has not had an occasion to consider a rejection based on an improper Markush group.

FN4. We use the phrase "one invention" to refer to a single patentable invention. We use the phrase "multiple inventions" to mean two or more inventions which are patentably distinct inventions within the meaning of 37 CFR § 1.601(n) (2001). We have expressly avoided using such terms as "independent" and "distinct" which appear in 35 U.S.C. § 121 and other terms which relate to criteria for making a "restriction" requirement. As the CCPA notes in Harnisch, rejections based on "restriction" requirements and rejections based on improper Markush groups stand on a different footing.

FN5. The CCPA decided, and the Federal Circuit now decides, cases and controversies on the precise facts of the case. On the other hand, the Congress in its legislation function, and the PTO in its rulemaking function, make policy decisions not necessarily limited to the facts of a given case. Hence, no one should fault the CCPA for not discussing all possible policy options in its Harnisch opinion.

FN6. Inasmuch as the R^1 is phenyl embodiment of claim 1 was examined on the merits as a result of a requirement for election of species, we will note that further examination may be necessary as to other R^1 embodiments, including the piperidinyl embodiment.

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